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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/577,601	05/25/2000	Sheena M. Loosmore	1038-1026 MIS:jb	6428

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/577,601	LOOSMORE ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *13 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5 and 8-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5 and 8-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. In the prior action, mailed on July 13, 2004, claims 4-6, and 8-12 were pending, under consideration, and rejected. In the Response filed on January 13, 2005, the Applicant amended claims 5 and 8, and cancelled claims 4 and 12.

2. Currently, claims 5, and 8-11 are pending and under consideration.

3. Because this action raises new grounds of rejection not necessitated by amendment, the action is made Non-Final.

Claim Rejections - 35 USC § 112

4. **(Prior Rejection- Withdrawn)** Claims 5, 6, 8-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on expression vectors encoding "a non-proteolytic analog of a Haemophilus Hin47 protein." It is not clear what is meant by the term "analog" in the claims. In view of the amendment of the pending claims such that they read on vectors encoding specific mutants of the Hin47 protein, the rejection is withdrawn.

5. **(Prior Rejection- Withdrawn)** Claim 8 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the claim was dependant on claim 7, which was cancelled from the application. In view of the amendment of claim 8 such that it now depend from claim 5, the rejection is withdrawn.

6. **(Prior Rejection- Withdrawn)** Claims 4 and 12, drawn to inventions comprising plasmids identified by their alpha-numerical designations, were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In view of the cancellation of these claims, the rejection is withdrawn.

7. **(Prior Rejection- Withdrawn)** Claims 4 and 12, drawn to inventions comprising plasmids identified by their alpha-numerical designations, were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In view of the cancellation of these claims, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. **(Prior Rejection- Maintained)** Claims 5, 6, and 8 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Bass et al, J. Bacteriology (Bass), 178:1154-61, in

view of the 1998 article (Loosmore et al., Infection and Immunity, 66(3): 899-906), and U.S. Patent number 5,474,914, issued to Richard Spaete (the Spaete patent). The claims read on expression vectors for expression of a recombinant protein comprising nucleic acids encoding a non-proteolytic mutant of the Hin47 protein (with substitutions at one of positions 91, 121, or 197), an additional recombinant protein, and comprising a regulatory element operatively connected each of the nucleic acids. The claims have been amended such that the nucleic acids encoding the Hin47 mutant includes the region encoding the protein's leader sequence.

Claim 6 has been cancelled from the application. The rejection is therefore withdrawn from this claim.

The Applicant presents two new grounds of traversal of the rejection. First, the Applicant argues that the prior art does not teach the inclusion of the leader sequence as required by the amended claims. Second, the Applicant argues that the art does not provide adequate teachings to provide for a reasonable expectation of success. These arguments are not found persuasive.

With respect to the first ground of traversal, the inclusion of the leader sequence, the Applicant argues that neither the teachings of Loosmore or Spaete render obvious the inclusion of the Hin47 leader sequence. This argument is not found persuasive. The Examiner agrees, as was indicated in the action mailed on February 25, 2003 (pages 14-15), that the Loosmore reference does not alone teach or suggest the inclusion of the leader sequence. However, while Spaete indicates that a chimeric DNA comprising a leader sequence may be used where the protein is to be expressed in a yeast, it would be recognized by those in the art that the naturally occurring leader sequence of Hin47 would be effective as a functional equivalent of the leader sequences of Spaete if the vector was to be expressed in a bacterium. In such a system, the

bacterial cell would be able to naturally process the leader sequence of Hin47, and would not require the artificial processing sites suggested for use in the yeast expression system of Spaete. Thus, while neither of the references specifically teaches the use of the Hin47 leader sequence, the teachings of Spaete suggest the inclusion of such a sequence. From the disclosure of Loosmore, disclosing the leader sequence of Hin47 as a signal sequence, it would have been apparent to those in the art that the native Hin47 leader sequence would be functional equivalent of the chimeric sequences of Spaete when used in bacterial cells. The first argument in traversal is therefore not found persuasive.

The second argument in traversal by the Applicant is that the art does not provide adequate teachings to provide a reasonable expectation of success in the use of the non-proteolytic Hin47 as a chaperone. These arguments are noted. However, they are not found persuasive in view of specific teachings in the art indicating that the non-proteolytic Hin47 mutants may be used as carriers for recombinantly expressed proteins. See e.g., U.S. Patent 5,656,436 (column 7, lines 35-53), and WO 96/03506 (pages 3, 6, and 14-15, and claim 52). In view of these specific teachings regarding Hin47, and the previously sited teachings of Loosmore, and the other references describing HtrA proteins more generally, the Applicant's arguments are not found persuasive. The rejection is therefore maintained for the reasons above, and the reasons of record.

10. **(Prior Rejection- Maintained)** Claims 9 was rejected under 35 U.S.C. 103(a) as being unpatentable over Bass, in view of the 1998 article, and the Spaete patent, and further in view of Barenkamp and St. Geme III, Molecular Microbiology 19:1215-23 (Barenkamp), and U.S. Patent

Number 6,335,182 (the 182 patent). These claims describe a an expression vector encoding a non-proteolytic Hin47 analog, a regulatory element, and an additional nucleic acid molecule encoding for another recombinant protein, wherein that recombinant protein is the Haemophilus influenzae Hia protein. The Applicant has provided no additional grounds of rejection over those indicated above. The rejection is therefore maintained for the reasons above, and those of record.

11. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bass, the 1998 article, Spaete, and Barenkamp as applied above, and further in view of St. Geme et al. (WO 96/30519). Claim 10 is directed to the claimed expression vectors wherein the recombinant polypeptide is an N-terminally truncated Hia protein.

The teachings of over Bass, the 1998 article, Spaete, and Barenkamp have been described above. As indicated above, these references render obvious the claimed vectors wherein the recombinant polypeptide is Hia. However, the references do not teach or suggest the use of a N-terminally truncated Hia protein. St. Geme teaches additional antigens against H. influenzae. The reference indicates that the protein identified as HA1 in the reference is the same as the hia reference in the art. Page 10, lines 2-3. The reference additionally teaches that fragments of the protein may be used, including N-terminal and C-terminal deletions, and indicates that a useful antigen comprises the C-terminal 120 residues (i.e. a N-terminally truncated fragment of Hia). Pages 12-13. It would therefore have been obvious to those in the art to use such a fragment of the Hia protein as the encoded recombinant polypeptide in the inventions suggested by the four previously cited references. The combination of these references therefore renders the claimed invention obvious.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. **(New Rejection)** Claims 5 and 8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10, 17, 19 of U.S. Patent No. 5,939,297. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the present application represent an obvious variation to the nucleic acids of the copending application. In particular, the present claims are directed to a nucleic acid encoding a non-proteolytic Hin47 and a second protein. The claims of the patent are directed to nucleic acids comprising a portion encoding the Hin47. Additionally, claim 34 of the patent, as well as lines 42-60 of column 7 of the specification clearly indicate that the "comprising" language of the indicated patent claims is intended to include embodiments wherein the nucleic acids encode a fusion protein comprising the mutant Hin47, and a second (recombinant) protein.

Further, the claims also indicate that the nucleic acid encoding the mutant Hin47 include mutant forms of the full length Hin47 gene- thus, including the leader sequence. See, claim 19. In view of these teachings of the patent, the current application reads on overlapping subject matter with the patent claims, the overlapping subject matter representing obvious variations of the nucleic acids of the patent claims.

14. **(New Rejection)** Claims 5 and 8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 5, and 6 of U.S. Patent No. 6,025,342. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the present application represent an obvious variation to the nucleic acids of the copending application. In particular, the present claims are directed to a nucleic acid encoding a non-proteolytic Hin47 and a second protein. . The claims of the patent are directed to immunogenic compositions comprising nucleic acids comprising a portion encoding non-proteolytic mutants of Hin47. Additionally, lines 3-6 and 25-43 of column 8 of the patent specification indicate that such compositions would include embodiments wherein the nucleic acids encode a fusion protein comprising the mutant Hin47, and a second (recombinant) immunogenic protein or peptide.

Additionally, the specification of the application indicates that the nucleic acid may include mutant versions of the full length Hin47 gene; thus, on nucleic acids including the leader sequence. Column 3. In view of these teachings of the patent, the current application reads on overlapping subject matter with the patent claims, the overlapping subject matter representing obvious variations of the nucleic acids of the patent claims.

15. **(New Rejection)** Claim 9 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over either claims 1, 5, and 6 of U.S. Patent No. 6,025,342 or claims 10, 17, 19 of U.S. Patent No. 5,939,297 as applied above, further in view of Barenkamp and St. Geme III, Molecular Microbiology 19:1215-23. Claim 9 describes the claimed expression vector wherein the additional nucleic acid molecule encodes a Hia protein of H. influenzae. As indicated above, the claims of both of the cited patents read on the claimed nucleic acids. Additionally, the specifications of each of these patents indicate that the claims include embodiments wherein the claimed nucleic acids also encode an additional immunogenic peptide which uses the mutant Hin47 as a carrier. Barenkamp teaches that the Hia protein may also be used as a vaccine against Haemophilus influenzae, especially in combination with other antigens. Pp. 1220-21. Thus, it would have been obvious to one of ordinary skill in the art to combine the Hin47 analog and Hia to make a multiantigenic vaccine for Haemophilus influenzae. Knowing that the two proteins could be used together, it would have been obvious to one of ordinary skill in the art to make an expression system that produces both antigens. Thus, based on the references above, it would therefore have been obvious to one of ordinary skill in the art to make an expression vector encoding both the Hin47 analog and Hia.

Conclusion

16. No claims are allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel 2/7/05

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